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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,233	10/24/2003	Zehra Kaymakcalan	BBI-190RCE	1420

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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
SKELDING, ZACHARY S	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,233	KAYMAKCALAN ET AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-11,15-17,21-24,28,29,31-36,40-45,48 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-11,15-17,21-24,28,29,31-36,40-45,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/18/05; 4/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 14, 2006 has been entered.

2. Applicant's amendment to the claims, filed April 14, 2006, has been entered.

   Claims 1, 4, 8, 11, 15, 17, 21, 23, 28, 31-36, 40, 42 and 48 have been amended.

   Claims 5-7, 12-14, 18-20, 25-27, 30, 37-39, 46 and 47 have been canceled.

   Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31-36, 40-45 and 48-49 are pending.

   Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31-36, 40-45 and 48-49 are under examination as they read on a method for treating rheumatoid arthritis by administering anti-TNFα antibodies.

3. This Office Action is in response to Applicant's amendment to the claims and remarks filed April 14, 2006.

   The rejections of record can be found in the previous Office Actions, mailed February 7, 2005 and October 21, 2005.

4. The prior rejection under 35 U.S.C. § 112, 2nd paragraph has been withdrawn in view of Applicant's amended claims filed April 14, 2006.

   The prior rejection under 35 U.S.C. § 112, 1st paragraph, enablement, has been withdrawn in view of Applicant's amended claims filed April 14, 2006.

   The prior rejection under 35 U.S.C. § 112, 1st paragraph, written description, has been withdrawn in view of Applicant's amended claims filed April 14, 2006.

5. Applicant's Information Disclosure Statement filed April 14, 2006 has been considered. Applicants are reminded that the author name should appear in all capital letters for the non-patent literature citations.

6. Applicant's submission of April 14, 2006 of references C1-D4 cited in the Information Disclosure Statement filed January 18, 2005 is acknowledged. A copy of the Information Disclosure Statement filed January 18, 2005 has been initialed and is provided to Applicants herewith.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

This is a New Grounds of Rejection. Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31-36, 40-45 and 48-49 are rejected under **35 U.S.C. 112, first paragraph,** as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for a **"dose of 0.01 – 0.1 mg/kg"** of anti-TNFα antibody to treat "a disorder in which TNFα activity is detrimental", such as arthritis or rheumatoid arthritis, or the symptoms associated therewith. This is a **New Matter** rejection based on Applicant's amended claims filed April 14, 2006.

Applicant's amendment filed April 14, 2006 does not provide sufficient direction for the written description for the above-mentioned amendment. Applicant points to page 19, first paragraph lines 11-13; table 2 at page 29 and Figure 5 in support of the above-mentioned amendment.

Applicant is claiming a subgenus not sufficiently supported by the specification as-filed. A generic or a sub-generic disclosure cannot support a species unless the species is specifically described. One of skill in the art would not consider use of a **"dose of 0.01 –0.1 mg/kg"** of anti-TNFα antibody to treat "a disorder in which TNFα activity is detrimental", such as arthritis or rheumatoid arthritis, or the symptoms associated therewith to be sufficiently supported by the disclosure of the instant specification. See M.P.E.P. 2163.05.

The specification as filed does not provide a sufficient written description of a **"dose of 0.01 –0.1 mg/kg"** of anti-TNFα antibody to treat "a disorder in which TNFα activity is detrimental", such as arthritis or rheumatoid arthritis, or the symptoms associated therewith. The specification does not provide blazemarks nor direction for claims reciting a **"dose of 0.01 –0.1 mg/kg"**. This limitation, which was not clearly disclosed in the specification as-filed, changes the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to point out where the instant specification provides sufficient written support for a **"dose of 0.01 –0.1 mg/kg"** of anti-TNFα antibody to treat "a disorder in which TNFα activity is detrimental", such as arthritis or rheumatoid arthritis, or the symptoms associated therewith. See MPEP 714.02 and 2163.06.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31-36, 40-45 and 48-49 stand rejected under **35 U.S.C. 102(b)** as anticipated by Salfeld et al. (US Patent No. 6,258,562; see entire document), for the reasons of record put forth in the prior Office Actions.

Applicant's arguments have been fully considered but have not been found convincing, essentially for the reasons of record put forth in the prior Office Actions.

Applicant argues that Salfeld et al. does not anticipate the instantly claimed invention because, while Salfeld "touches" the claimed range, Salfeld allegedly fails to disclose a specific example falling within the claimed range, because the instant claims are directed to a dosage range that is narrower than the range taught by Salfeld, and because the instant specification discloses the unexpected result that the dosage range recited in the instant claims is effective in treating disorders in which TNFα is detrimental, such as rheumatoid arthritis.

Applicant also refer to M.P.E.P. § 2131.03 section II, which is reproduced below for reference (***emphasis added***):

> **II. PRIOR ART WHICH TEACHES A RANGE WITHIN, OVERLAPPING, OR TOUCHING THE CLAIMED RANGE ANTICIPATES IF THE PRIOR ART RANGE DISCLOSES THE CLAIMED RANGE WITH "SUFFICIENT SPECIFICITY"**
>
> When the prior art discloses a range which touches, overlaps or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. ***In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute."*** What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims. The unexpected results may also render the claims unobvious. ***The question of "sufficient specificity" is similar to that of "clearly envisaging" a species from a generic teaching.*** See MPEP § 2131.02. A 35 U.S.C. 102/ 103 combination rejection is permitted if it is unclear if the reference teaches the range with "sufficient specificity." The examiner must, in this case, provide reasons for anticipation as well as a motivational statement regarding obviousness. *Ex parte Lee*>,< 31 USPQ2d 1105 (Bd. Pat. App. & Inter. 1993) (expanded Board). For a discussion of the obviousness of ranges see MPEP § 2144.05.

Applicant's argument is not found persuasive because the instantly claimed invention is taught by Salfeld et al. with ***"sufficient specificity to constitute an anticipation under the statute."*** More particularly, Salfeld teaches dosage of anti-TNFα antibody, or an antigen binding portion thereof within the range of 0.1-20 mg/kg, is effective for treating rheumatoid arthritis. The effective dose range "0.1-20 mg/kg" ***recites the discrete dosage value of "0.1" which is also recited in the instant claims.*** As stated above, "The question of 'sufficient specificity' is similar to that of "clearly envisaging" a species from a generic teaching", and in the present situation, one of skill in the art reading Salfeld would not only "clearly envisage", but would instantly recognize that "0.1" mg/kg is an effective dose of anti-TNFα antibody, or an antigen binding portion thereof for treating rheumatoid arthritis.

Applicant's arguments that the claimed range is narrower than the range taught by Salfeld, and that the dose range recited in the instant claims is unexpectedly effective in treating disorders in which TNFα is detrimental, such as rheumatoid arthritis, does not negate the fact that the effective dose range of Salfeld, "0.1-20 mg/kg", ***recites the discrete dosage value of "0.1" which is also recited in the instant claims***, and thus Salfeld anticipates the instant claims.

It is noted that the functional properties of the anti-TNFα antibody (e.g. as recited in claim 41) are inherent properties of the D2E7 antibody taught by Salfeld et al. It is further noted that treatment of specific symptoms of rheumatoid arthritis (e.g. as recited in claim 43) is inherent to the treatment of rheumatoid arthritis as taught by Salfeld et al.

10. Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31-36, 40-45 and 48-49 stand rejected under **35 U.S.C. 102(e)** as anticipated by Salfeld et al. (US Patent No. 6,509,015; see entire document), for the reasons of record put forth in the prior Office Actions.

Applicant's argument has been fully considered but has not been found convincing, essentially for the reasons of record put forth in the prior Office Actions.

Applicant arguments are essentially the same as those set forth in response to the rejection under 35 U.S.C. 102(b), and have been addressed in Section 9 supra.

11. **This is a New Grounds of Rejection.** Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31 and 43 are rejected under 35 U.S.C. § 102(b) as anticipated by Adair et al. (U.S. Patent No. 5,994,510, citation B1 on Applicant's IDS of January 18, 2005)(see entire document).

Adair et al. teach a method of treating a disorder in which TNFα activity is detrimental, for example rheumatoid arthritis, and the symptoms associated therewith, comprising administering an anti-TNFα antibody, for example CDP571, or an antigen binding portion thereof, as a stand alone agent or with an additional therapeutic agent. (See entire document, in particular column 11, lines 19 through column 12, line 61; columns 14-17, Examples 1-2; and column 8, lines 53-64).

Adair further teaches at column 12, lines 36-55 (emphasis added), "the dose at which the antibody is administered depends on the nature of the condition to be treated, the degree to which the TNF to be neutralised is, or is expected to be, raised above a desirable level, and on whether the antibody is being used prophylactically or to treat an existing condition. The dose will also be selected according to the age and conditions of the patient. Thus, for example, where the product is for treatment or prophylaxis of septic shock suitable doses of antibody to TNF lie in the range **0.001**-30 mg/kg/day, preferably **0.01**-10 mg/kg/day and particularly preferably **0.1**-2 mg/kg/day."

Thus, Adair anticipates the instantly claimed invention.

It is noted that although the elected species of disease to be treated is rheumatoid arthritis, this reference anticipates not only the elected species of disease to be treated but also other species encompassed by the instantly claimed genus "a disorder in which TNFα activity is detrimental".

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

    A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

    Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. **This is a New Grounds of Rejection.** Claims 1-4, 8-11, 15-17, 21-24, 28, 29, 31-36, 40-45 and 48-49 are rejected/provisionally rejected, under the judicially created doctrine of **obviousness-type double patenting** as being unpatentable over:

    A. claims 1–100 of U.S. Patent No. 6,509,015;

    B. claims 15-19 of copending Application USSN 11/233,252; and

    C. claims 114-121 and 141-166 of copending Application USSN 09/801,185

    each in view of Salfeld et al. (US Patent No. 6,258,562, see entire document) and Adair et al. (U.S. Patent No. 5,994,510, see entire document). Although the conflicting claims are not identical, they are not patentably distinct from each other.

    It is noted that the elected invention in the instant application is limited to a method of treating rheumatoid arthritis; however, certain claims of U.S. Patent No. 6,509,015, and copending Applications USSN 11/233,252 and USSN 09/801,185, read on other diseases and so are also included in this rejection because they anticipate the instant claims drawn to the genus of ***all*** "disorders in which TNFα activity is detrimental".

    Claims 1–100 of U.S. Patent No. 6,509,015 are directed to a method of treating rheumatoid arthritis by administering an anti-TNFα antibody, alone or in combination with additional therapeutic agents. The patent clarifies, e.g. in columns 2-3 bridging paragraph, that the claimed methods employ antibody D2E7, i.e. the same antibody as recited in the instant claims.

Claims 15-19 of copending Application USSN 11/233,252 are directed to a method of treating rheumatoid arthritis by administering an anti-TNFα antibody, alone or in combination with additional therapeutic agents. The specification clarifies e.g. on page 3, 2nd paragraph, that the claimed methods employ antibody D2E7, i.e. the same antibody as recited in the instant claims.

Claims 114-121 and 141-166 of copending Application USSN 09/801,185 are directed to a method of treating rheumatoid arthritis by administering an anti-TNFα antibody, alone or in combination with additional therapeutic agents. The specification clarifies e.g. on page 3, 3rd paragraph, that the claimed methods employ antibody D2E7, i.e. the same antibody as recited in the instant claims.

Since treatment of the same disorder is claimed in U.S. Patent No. 6,509,015, and copending Applications USSN 11/233,252 and USSN 09/801,185, as in the instant application, i.e., rheumatoid arthritis, the symptoms of the disorder are inherently the same, and therefore are not patentably distinct from the instant claimed invention.

The instant claims differ from the reference teachings in the recitation of a "dose of 0.01 – 0.1 mg/kg."

Salfeld teaches the use of an anti-TNFα antibody, for example D2E7 (see entire document, in particular column 4, lines 42-67) or infliximab, also known as "cA2" (see, in particular column 23, line 24 and column 28, lines 65-67), or an antigen binding portion thereof, to treat rheumatoid arthritis, wherein an effective dose of anti-TNFα antibody is for example, within the range of 0.1-20 mg/kg (see entire document, in particular and column 26, lines 26-37).

Adair teaches the use of anti-TNFα antibody, for example CDP571, or an antigen binding portion thereof, to treat rheumatoid arthritis, wherein an effective dose of anti-TNFα antibody is for example, 0.001 or 0.01-10 or 0.1 mg/kg (see entire document, in particular column 11, lines 19 through column 12, line 55).

One of skill in the art would have been motivated to combine a method of treating rheumatoid arthritis by administering an anti-TNFα antibody, for example the D2E7 or infliximab antibodies, alone or in combination with additional therapeutic agents, as taught by U.S. Patent No. 6,509,015, and copending Applications USSN 11/233,252 and USSN 09/801,185, with the teachings of Salfeld because Salfeld also teaches that an anti-TNFα antibody, for example the D2E7 or infliximab antibodies, or an antigen binding portion thereof, can be used to treat rheumatoid arthritis, ***and further teaches*** that an effective dose of anti-TNFα antibody is for example, 0.1 mg/kg, and with the teachings of Adair, because Adair also teaches that an anti-TNFα antibody, for example the CDP571 antibody, or an antigen binding portion thereof, can be used to treat rheumatoid arthritis, and ***further teaches*** that an effective dose of anti-TNFα antibody is for example, 0.001, 0.01 or 0.1 mg/kg.

Given the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

With respect to copending Applications USSN 11/233,252 and USSN 09/801,185, this is a **provisional** obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PHILLIP GAMBEL, PH.D . JD
PRIMARY EXAMINER
TC 1600
7/10/06

Zachary Skelding, Ph.D.
Patent Examiner
July 8, 2006